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10/089,549	04/01/2002	Michio Kubota	KUBOTA=9	3265

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/089,549	KUBOTA ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,48 and 52-54* is/are pending in the application.

4a) Of the above claim(s) *1,48 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 53* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 48, 52-54 are currently pending and are present for examination. Claims 3, 53-54 are now under consideration. Claims 1, 48, 52 remain withdrawn from consideration as being drawn to non-elected invention.

Applicants' amendments and arguments filed on 8-1-06, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Examiner's suggestion made to applicants in a telephone call on 12-8-06 and 12-13-06, to amend claims 54 and 3 such that they both depend from claim 53 leading towards an allowance failed to be persuasive. Applicants declined to accept Examiner's suggestion.

Claim Objections

Claim 53 is objected to because of the following informalities: Claim 53 lists the characteristics such as Molecular weight and isoelectric points as "136,000 + 20,000 Daltons.." and "about 7.3 + 0.5" respectively. However this is incorrect. Originally applicants had presented the same characteristics as "136,000 $\pm$ 20,000 Daltons.." and "about 7.3 $\pm$ 0.5" respectively indicating the "plus or minus" symbol as opposed to only the "plus" symbol in the current version of the claim. Examiner has assumed that this is a typographical error and therefore has not rejected the claim for presenting new matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54, 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 54 recites the phrase "which enzyme has a partial amino acid sequence of SEQ D NO:1, 11, or 18 as a partial amino acid sequence..." in lines 9-10. It is still not clear to the Examiner whether the claimed enzyme has a subsequence of SEQ ID NO:1, 11 or 18 or that the amino acid sequences SEQ D NO:1, 11 or 18 are indeed the partial sequence of the claimed enzymes. Examiner requests clarification.

In response to the previous Office action, applicants have amended claim 54 by introducing the phrase "as a partial amino acid sequence" which has indeed made the whole phrase more confusing. Perhaps it will be more definitive if applicants delete the phrase the first time recitation of the phrase "a partial amino acid sequence of" in the above phrase so that it reads as "...which enzyme has SEQ ID NO:1, 11 or 18 as a partial amino acid sequence;...".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54, 3, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a native α –isomaltosylglucosaccharide forming enzyme wherein said enzyme is specifically isolated from a wild type non-recombinant *B.globisporus* N75 strain deposited as FERM BP-7591 and mutants thereof, having the following characteristics such as a Molecular weight of about 136,000 ± 20,000 Daltons on SDS-PAGE; an Isoelectric point of

about 7.3 $\pm$ 0.5 on isoelectrophoresis using ampholine; optimum temperature (i) About 50 degree C when incubated at a pH of 6 for 60 minutes; about 55 degree C when incubated at a pH of 6.0 for 60 minutes in the presence of 1 mM Ca ; an optimum pH about 6.0 when incubated at 35 degree C for 60 minutes; thermal stability (i) stable up to a temperature of about 45 degree C when incubated at a PH of 6.0 for 60 minutes; (ii) stable up to a temperature of about 50 degree C when incubated at a pH of 6.0 for 60 minutes in the presence of 1mM Ca ; pH stability; Stable at pHs of about 5.0 to about 9.0 when incubated at 4 degree C for 24 hours and consisting of the amino acid sequences SEQ ID NO:1, 11 or 18 does not reasonably provide enablement for any such enzyme from any source including a recombinant *B.globisporus*, or variants and mutants of such enzymes comprising the partial amino acid sequence of SEQ ID NO:1, 11, or 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 54, 3, are so broad as to encompass any α –isomaltosylglucosaccharide forming enzymes from any source comprising partial amino acid sequence of SEQ ID NO:1, 11 or 18 and having any physicochemical properties including variants, mutants and recombinants. The scope of the claims is not commensurate with the enablement provided by the disclosure with

regard to the extremely large number of α –isomaltosylglucosaccharide forming enzymes broadly encompassed by the claims including mutants, variants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single native α –isomaltosylglucosaccharide forming enzyme isolated from *B.globisporus* N75, FERM BP-7591 and consisting of amino acid sequence SEQ ID NO:1,11 or 18. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of the native enzyme isolated from *B.globisporus* N75, FERM BP-7591 as a α –isomaltosylglucosaccharide forming enzyme but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass α –isomaltosylglucosaccharide forming enzymes from any or all sources including mutants, variants and recombinants because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its specific activity; (B) the general tolerance of α –isomaltosylglucosaccharide forming enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in the amino acid sequence of the enzyme with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including α –isomaltosylglucosaccharide forming enzymes with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of α –isomaltosylglucosaccharide forming enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In their response to the previous Office action, applicants have traversed the above rejection arguing that there is support for the sequences of SEQ ID NO:1, 11, and 18, in the specification as originally filed at page 33, line 8 and claim 5 and therefore the rejection must be withdrawn. Examiner respectfully disagrees with such an argument as being persuasive to overcome this rejection. While the specification may have support for SEQ ID NO:1, 11, and 18, applicants should keep in mind that these sequences are partial sequences limited to short stretches of amino acids with the remaining structure unknown and furthermore these sequences are isolated from one specific source. However, the polypeptides claimed are NOT limited to just those polypeptides recited in the specification but reads on all variants, mutants and recombinants from any or all sources. Furthermore, while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for making and selecting only those from the infinite number of variants that have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in

which the experimentation should proceed. Such guidance has not been provided in the instant specification. Hence the above rejection is maintained.

Claims 54, 3, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polypeptides having α –isomaltosyl-glucosaccharide forming activity and comprising one of the short amino acid sequences SEQ ID NO:1, 11 or 18. The specification does not contain any disclosure of the full structure of all the amino acids sequences included in the claimed genera. The genus of polypeptides claimed is a large variable genus with the potentiality of having many different structures. Therefore, many structurally distinct polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by amino acid sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus (i.e., partial amino acid sequences SEQ ID NO:1, 11 or 18) does not constitute a substantial portion of the genus as the remainder of the structure of the polypeptide having α –isomaltosylglucosaccharide forming activity is completely undefined and the specification does not define the remaining structural

features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing that claim 54 has been amended to recite that the enzyme contains a partial amino acid sequence of SEQ ID NO:l, 11 or 18 and coupled with the physicochemical characteristics of the enzyme, this information should be sufficient information to describe the enzyme claimed herein. Examiner respectfully disagrees with such an argument as being persuasive to overcome this rejection. This is because, even though the claim describe the functional characteristic of the enzyme they fail to address the full structure of the enzyme. It must be noted here that the amino acid sequences that limit the enzymes are not full-length sequences but are short stretches. The remaining structure of amino acid sequence remains unknown. Furthermore, there is no information either in the art or in the specification that discloses that the structure of SEQ ID NO:1, 11 or 18 are representative of the entire genus of the enzymes claimed. Examiner reiterates that providing just the partial structure of the claimed enzyme does not remedy the written description issue in these claims. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., full structure or other

physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of enzymes includes species which are widely variant in structure. The genus claims 54 and 3 is structurally diverse as it encompasses polypeptides from any or all sources including variants, mutants and recombinants but having a singular function. As such, neither the description of a partial structure coupled with functional nor the disclosure solely of functional characteristics present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Therefore the above rejection is maintained.

Conclusion

Claim 53 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and

any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

December 13, 2006